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Population-Based Study of Men of African Descent

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13. ABSTRACT (Maximum 200 Words) We hypothesized that the elevated risk for prostate cancer, observed in African Americans compared with whites, is present in all populations of African descent suggesting that genetic and/or shared metabolic and lifestyle factors, rather than environmental factors, are the main determinants of elevated risk. We recruited 1088 males (95% Afro-Caribbean), aged 40-90 on the island of Tobago, Trinidad & Tobago. Among 798 men with screening results, aged 50-79, serum prostate specific antigen (PSA) was elevated (≥ 4 ng/ml) in 31%, digital rectal exam abnormal in 25%, and either abnormal in 41%. Prostate cancer was diagnosed in 102 of 208 men undergoing biopsy. The positive predictive value (PPV) for elevated PSA was 55%. Few of the tumors (14%) were of advanced Gleason grade (8-10); 86% Gleason grade 5-7. No tumors of grade 1-4 were observed. The prevalence of screening-detected cancer was 13.4% of men aged 50-79. Elevated PSA rates, PPV for PSA, and prevalence of prostate cancer, were all much higher than observed in early screening studies in predominantly Caucasian populations. We conclude that this population has a high risk for prostate cancer, as observed in African Americans. Case control studies of genetic markers, and lifestyle and environmental factors are beginning.				
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FOREWORD

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 Nov 29, 1999
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Table of Contents

Cover Sheet	1
SF 298	2
Foreword	3
Table of Contents	4-5
Introduction	6
Statement of Work	6
Discussion of Screening Results	8
Key Research Accomplishments	10
Reportable Outcomes	11
Conclusions	12
References	13
Appendix	14
Tables	
Table 1. Tobago Prostate Survey - Annual Summary, Year 1, ending Nov. 1, 1999.	
Table 2. Positive Predictive Value of PSA and DRE in Tobago	
Figures	
Figure 1. Percent with Elevated PSA (≥ 4 gn/ml) in Tobago Compared with Early U.S. Screening Studies.	
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2. Bunker C. Epidemiology of Prostate Cancer in Populations of African Descent. Presented at A Symposium on Prostate Cancer, University of Pittsburgh Medical Center, June 19, 1999. Target audience: African American clinicians and the general public. (Appendix)

Manuscript.

1. Bunker CH, Patrick AL, Brufsky AM, Vivas CA, Dhir R, Konety BR, Becich MJ, Trump DL, Kuller LH. High Prevalence of PSA Screening-Detected Prostate Cancer Among Afro-Caribbeans: Preliminary Results From the Tobago Prostate Cancer Survey. To be submitted to the Journal of Urology in December, 1999.

Introduction.

We hypothesized that the elevated risk for prostate cancer, observed in African Americans compared with whites, is present in all populations of African descent suggesting that genetic and/or shared metabolic and lifestyle factors, rather than environmental factors, are the main determinants of risk. In Phase I, we are testing this hypothesis by determining whether the prevalence of prostate cancer in the male population, aged 50-79, of the Caribbean island of Tobago (92 percent of African descent) is similar to or greater than the prevalence in the African American population. An island-wide screening and surveillance system has been established. We estimated that there are 2931 ambulatory, free living men aged 50-79, and that 2346 (80%) will participate. The population is being screened using PSA and digital rectal exam (DRE). Participants with positive PSA (≥ 4 ng/ml) or abnormal DRE are undergoing biopsy for diagnosis of prostate cancer. Also in Phase I, we will conduct pilot studies to explore hypotheses regarding several new measures of possible risk factors for prostate cancer in biopsy positive vs biopsy negative participants. These include serum arachidonic acid (may be modulated by dietary meat and fat intake, hypothesize high levels related to prostate cancer), metabolic (bone mineral density as a surrogate for lifetime sex hormone exposure, hypothesize high bone density related to prostate cancer), and genetic factors (frequency of specific alleles in genes for the androgen receptor, vitamin D receptor, 5-alpha reductase). This large, cooperative, black male population provides a uniquely valuable opportunity for the study of prostate cancer risk. Understanding the contribution and interaction of environmental, genetic and metabolic factors should enable us to reduce the risk for prostate cancer among men of West African descent.

Statement of Work.

Task 1. Initiation of study (Months 1-3)

- a. Order supplies.*
- b. Pre-test questionnaires and study procedures on Tobago male volunteers, modify procedures as required, and secure approval of modifications from Institutional Review Board.*
- c. Recruit and train Pittsburgh and Tobago staff.*
- d. Setup data files and data entry procedures.*
- e. Produce and distribute recruitment materials.*

Task 1a. Supplies for the first year were ordered, received, and transported to Tobago.

Task 1b. The questionnaires, which had already undergone pilot testing, proved to be adequate and have not been further modified since the Surgeon General IRB.

Task 1c. Extensive training effort has been completed.

Drs. Bunker and Patrick trained the Tobago recruiters, data collectors, lab personnel, and nurses. A University of Pittsburgh urologist trained urologists and surgeons in the DRE protocol, January, 1999.

Task 1d. Data files and data entry procedures are established. The recruitment log data, record of blood draw, shipping log, digital record exam, and biopsy completion are entered in Tobago and e-mailed to Pittsburgh where they are merged into a participant management file which is e-mailed to Tobago. The baseline questionnaire, PSA results, biopsy results, and freezer data base are entered and managed in Pittsburgh. The PSA results and biopsy results are e-mailed to Tobago as soon as they are received from the laboratory.

Task 1e. Recruitment materials have not yet been needed to stimulate recruitment, so production and distribution has not been implemented.

Task 2. Conduct PSA & DRE screening for prostate cancer in Tobago male population aged 50-79, Mons 4-17.

a. Recruit and screen about 170 participants per month beginning in St. David county.

b. Provide screening results to participants within two months of screening visit by letter (normal results) or informing visit (abnormal results).

Task 2a. Recruitment. Table 1 (Appendix) shows recruitment and screening by age group as of November 1, 1999. The response to the study has been astonishing. 1088 men have volunteered, age <40 - 90+. The recruitment target age was 50-79. However, as we noted in the application, we did intend to accept volunteers outside of this age group in the interest of public relations. Demand has fallen off in the over age 79 group (4% of recruits in year 1). However, demand is strong and growing in the under age 50 group (21% of recruits in year 1). As a result, we applied for, and have just received separate funding (see below), to support recruitment and screening in the age 40-49 year old group. Because of the strong volunteer pressure, we have not yet instituted systematic recruitment procedures by county. These procedures will be instituted as needed when volunteer pressure decreases. Recruitment is still picking up momentum (315 have been recruited since November 1).

Screening. (See Table 1, Appendix).

PSA Results. A 15 ml plain vacutainer of peripheral blood was drawn from fasting subjects. Aliquots of serum were frozen at -20°C for later measurement of PSA. Clots were frozen for later DNA studies. PSA assays are being done in the Central Pathology Laboratory, University of Pittsburgh Medical Center (UPMC), using the automated Microparticle Enzyme Immunoassay, Abbot AxSYM PSA assay (Abbott Laboratories, Abbott Park, IL, USA). PSA results have been received for 872 men. In men of all ages, 17% (234/872), and in men aged 50-79, 31% (209/679) of PSA results have been elevated (> 4 ng/ml).

DRE Results. DRE results have been abnormal in 23% (196/863) of men of all ages, and in 25% (160/657) of men aged 50-79. PSA and/or DRE were abnormal in 37% (322/872) of all men, and in 41% (279/679), age 50-79. Biopsy has been recommended for 320 men.

Biopsy Results. Trans-rectal ultrasound guided biopsy was performed using an 18 gauge, 21 cm spring-loaded biopsy needle (Boston Scientific, Natick MA). Random sextant biopsies, plus biopsy of suspicious nodules, were obtained according to a standard protocol. The formalin preserved specimens were stored at room temperature and shipped to the University of Pittsburgh Central Pathology Laboratory for histopathologic examination. The specimens were examined for presence or absence of high grade prostatic intra-epithelial neoplasia (PIN), presence or absence of cancer, Gleason score of cancer, location of cancer, and peri-neural invasion. Pathology results have been received for 208 men. One hundred and two men have been diagnosed with prostate cancer. The positive predictive value for abnormal DRE and/or elevated PSA is 49% in this population. Detailed data on positive predictive values for PSA \pm DRE are presented in Table 2 in the Appendix, and in the abstract.

Prevalence of Screening-Detected Prostate Cancer. Even with biopsy results not yet available for a third of referred group, 11.7% (102/872) of all screened men, and 13.4% (91/679) of screened men aged 50-79, have been diagnosed with prostate cancer. The actual rate will be higher when screening is completed for all recruited men, and when biopsies are completed for a larger

proportion of the referred men.

Discussion of Screening Results. This study, which we believe is the first involving screening a large Afro-Caribbean population, found high rates of elevated PSA (≥ 4 ng/ml), ranging from 14%, age 50-59, to 52%, age 70-79. Similar data from screening of other populations of African descent have not been published. In Figure 1, the Tobago data are compared with data from screening studies of predominantly Caucasian populations^{1 2 3} which were conducted between 1989-1992, when PSA screening was just beginning to be widely used in the United States. Age-specific rates of elevated PSA levels in Tobago were approximately double those observed in a large, predominantly Caucasian study in the United States by Ritchie et al.¹ In that volunteer population of 6,630 (92% Caucasian, 3% African American, 5% other), recruited by advertisement, mean age was 62.8 years, and 53% reported symptoms of prostatism. The proportion with elevated PSA ranged from 6.3% (150/2381) age 50-59, 16.5% (487/2959) age 60-69, to 26.8% (311/1611) in age 70-79 (See figure 1). The standardized rates of elevated PSA, based on the age distribution of the population reported by Ritchie et al., were 27.5/100, standard error 2.53/100 (95% confidence interval, 22.5-32.5/100) in the Tobago population, and 14.8%, standard error, 0.43/100 (95% confidence interval, 15.4-17.85/100) in the population reported by Ritchie et al.¹

As has been observed in African American populations, the positive predictive value of elevated PSA was high in the Tobago population among whom prostate cancer diagnosed in 49% of men undergoing biopsy. In a community based study of relatively young African Americans, aged 40+, mean age 54.9, PSA was over 4 ng/ml in 8% (85/1105)⁴. Prostate cancer was diagnosed in 36 of 81 (44%) undergoing biopsy. In a study of 752 men (age not specified) who had undergone biopsy for a history of elevated PSA (≥ 4 ng/ml), cancer rates were 54% (94/175) among blacks and 41% (122/197) among whites⁵. In the population of 6630 (92% Caucasian) population reported by Ritchie et al described above, among the participants with elevated PSA who underwent biopsy, 31% (216/686) over all ages were positive for cancer. The proportion with positive biopsy in that study varied little across age groups (range 29.5-33.8%).

These preliminary data strongly support our hypothesis that risk for prostate cancer is high in populations of African descent exposed to different environments. This strongly suggests that genetic and/or shared metabolic and lifestyle factors, rather than environmental factors, are the main determinants of elevated risk among populations of African descent. An earlier preliminary report of this finding of very high screening prevalence was presented at the annual meeting of the Caribbean Health Research Council, Barbados, April 24, 1999 (abstract and presentation in Appendix). An intermediate preliminary manuscript has been prepared (n=529 screened men) (see Appendix). In that manuscript, we addressed the issue of early self-referral bias (i.e. symptomatic men coming forward first) because the study population was not yet population based. However, when we excluded symptomatic men, and men with prior PSA testing, the prevalence of prostate cancer in the screened population remained at about 12%. Therefore, we do not believe that the self-referral bias has inflated the prevalence rate significantly. We are in the process of updating this manuscript to the current new dataset in this annual report. We intend to submit this to the Journal of Urology the first week in December, 1999,

Task 2b. We have not been able to provide results of PSA testing or biopsies to participants within 2 months as planned. This has been due to problems with sample transport. Biological sample shipment has become much more difficult and expensive in the past couple of years. DHL is only express shipper which will carry biological samples from Trinidad to the US. Shipments now prohibitively expensive, \$500-\$600 each. Also, DHL, though historically very reliable, lost one of our shipments (urines and clots) for eight days. Therefore, most of our samples have been stored in Trinidad for up to 3 months waiting for the opportunity for one of us to carry them to Pittsburgh as checked baggage. This means not only delayed shipment, but also the batches of PSAs and biopsies going to the labs are very large. These large batches bog down the system and cannot be processed with the usual fast turnaround time observed for small batches. Thus, provision of screening and biopsy results has taken about 1-4 months rather than the planned 1-2 months. We have been trying to negotiate two day air freight with individual airlines but so far have not found an alternative. Meanwhile, the situation is less than desirable, but it is working. Other types of medical tests which have to be sent off island also take a long time, so the delay does not seem too unusual to the men.

Task 3. Support Regional Health Authority in scheduling and completing biopsies and provide pathological diagnosis, Months 6-21.

- a. Schedule a concentrated 2-3 day session for doing biopsies every other month (60-70 biopsies per session).*
- b. Train local urologists/surgeons in biopsy protocol during the first and second of these bimonthly biopsy sessions.*

Task 3a, 3b. Trinidad has three practicing urologists and two surgeons with some urology training. Four of these five, plus two Tobago surgeons and Co-PI Dr. Patrick, have participated in ultrasound-guided, random sextant, biopsy two day training sessions conducted by University of Pittsburgh urologists on two occasions. Due to time constraints, none of the Trinidad physicians have been able to participate in regular biopsy sessions on Tobago. Instead, one biopsy session (usually 8-10 biopsies) a week is conducted by one of the two Tobago surgeons under the supervision of the Co-PI Dr. Patrick. This has worked very well. There have been no major complications. The high rate of cancer detection suggests that the surgeons are adhering well to the random sextant biopsy protocol.

Task 4. Support referral of patients for treatment for prostate cancer and follow up on treatment outcome, Months 8-30.

- a. Counsel patients diagnosed with prostate cancer regarding treatment options (estimate 145-200).*
- b. Conduct a one-day workshop for prostate cancer treatment providers and Health Authority officials in Trinidad and Tobago regarding prostate cancer treatment options.*
- c. Assist Tobago Regional Health Authority and patients with appropriate treatment referral.*
- d. Contact patients at six month intervals to determine vital status and treatment history; obtain medical records and death certificates.*

Task 4a. All patients diagnosed with prostate cancer have been counseled regarding treatment options by Co-PI, Dr. Alan Patrick.

Task 4b. A treatment workshop was conducted in January, 1999, in Tobago by a team of urologist, medical oncologist, epidemiologist from the University of Pittsburgh, and the Co-PI from Tobago. The audience of about 20 included the majority of clinicians on the island.

Task 4c. All men with prostate cancer have been referred to the general surgical clinic at the Tobago Hospital. This is the established referral practice for prostate cancer in government hospitals. We have held numerous meetings with the Secretary, Division of Health and Social Services, Tobago, the Administrator and Health Planner, Division of Health and Social Services, Tobago, the Tobago Hospital Administrator, the County Chief Medical Officer, health officials from Trinidad, Trinidad radiologists and urologists, and Tobago clinicians, to discuss planning and resources for prostate cancer treatment, included surgery, external beam radiation, and medical treatment. The officials are currently determining the feasibility of establishing a urology clinic at the Tobago Hospital twice a month.

Task 4d. Few men have had their diagnosis for six months. This followup is just now being instituted.

Task 5. Conduct pilot case control studies, Months 13-24.

a. Identification of first 50 cases with pathologically diagnosed prostate cancer, one age-matched control with elevated PSA but normal biopsy, and two age-matched controls for each case.

b. Measure serum arachidonic acid in cases and controls.

c. Determine androgen receptor, vitamin D receptor, 5-alpha-reductase receptor, and chromosome 1q24-25 genotypes in cases and controls.

d. Hand X-ray and bone mass estimation in cases and controls.

These studies are just beginning.

Task 6. Analysis of screening data and conventional risk factors, Months 18-24.

a. Data analysis and preparation of manuscripts regarding screening outcome.

b. Data analysis and preparation of manuscripts regarding conventional potential risk factors for prevalent prostate cancer in this population including central obesity, alcohol intake, vasectomy, occupation (particularly agriculture).

c. Preparation of annual report.

Task 6a. Preliminary abstracts and manuscripts have been prepared (See above, see Appendix).

Task 6b, 6c. These tasks have not begun.

Task 7. Analysis of pilot case-control data, Months 25-30

a. Analysis of data from case-control studies of bone-density, serum arachidonic acid, and genotyping, and preparation of brief manuscripts as appropriate.

b. Preparation of final report.

Tasks 7a, 7b. Data not yet available.

Key Research Accomplishments:

> Preliminary data strongly support a high risk for prostate cancer in the population of Tobago; screening prevalence of prostate cancer is 13.4% among men aged 50-79.

> The positive predictive value of elevated serum prostate specific antigen (PSA \geq 4 ng/ml) is very high in this West African descent population; 55% of biopsied men with elevated PSA have

been diagnosed with prostate cancer.

> The positive predictive value for abnormal digital rectal exam is similar to other populations.

> An ideal population has been identified for further study of factors contributing to the high risk of prostate cancer among men of West African descent.

Reportable Outcomes:

Abstracts.

1. Patrick AL, Bunker CH, Brufsky AM, Dhir R, Becich MJ. Preliminary screening results suggest high prevalence of prostate cancer in Tobago. Abstract accepted for the Annual Meeting of the Caribbean Health Research Council, April 21-24, 1999, Barbados. (Appendix)

2. Patrick AL, Bunker CH, Konety BR, Brufsky AM, Vivas CA, Dhir R, Becich MJ, Trump DL, Kuller LH. Positive Predictive Value of Prostate Specific Antigen (≥ 4 ng/ml) and Abnormal Digital Rectal Exam for Prostate Cancer on the Caribbean Island of Tobago. Submitted for Annual Meeting of the Caribbean Health Research Council, April 20-22, 2000, Port of Spain, Trinidad & Tobago. (Appendix)

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- patents and licenses applied for and/or issued; none.
- degrees obtained that are supported by this award; none.
- development of cell lines, tissue or serum repositories; none.
- informatics such as databases and animal models, etc; none.
- funding applied for based on work supported by this award;
R01 CA84950 Molecular Epidemiology of Prostate Cancer InTobagonians; application was submitted to NIH April 23, 1999; awarded Sept 29, 1999. This NIH grant application protocol and budget were carefully planned and written to extend and supplement the work in the DAMD contract. This grant extends the screened group to include men aged 40-49. Additional molecular markers will be studied. The large case-control study will include additional cases and controls. There is no budgetary overlap with DAMD 17-99-1-9015 (See Appendix for abstract, budget complementation table).
- employment or research opportunities applied for and/or received on experiences/training supported by this award; none.

Conclusions.

Elevated PSA rates, PPV for PSA, and prevalence of prostate cancer, were all much higher than observed in early screening studies in predominantly Caucasian populations. We conclude that this population has a high risk for prostate cancer, as observed in African Americans. This supports our hypothesis that the elevated risk for prostate cancer, observed in African Americans compared with whites, is present in other populations of African descent suggesting that genetic and/or shared metabolic and lifestyle factors, rather than environmental factors, are the main determinants of elevated risk. This large, cooperative, African descent male population provides a uniquely valuable opportunity for the study of prostate cancer risk. Understanding the contribution and interaction of environmental, genetic and metabolic factors should enable us to reduce the risk for prostate cancer among men of West African descent.

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Appendix.

Tables.

Table 1. Tobago Prostate Survey - Annual Summary, Year 1, ending Nov. 1, 1999.

Table 2. Positive Predictive Value of PSA and DRE in Tobago.

Figures.

Figure 1. Percent with Elevated PSA (≥ 4 gn/ml) in Tobago Compared with Early U.S. Screening Studies.

Funding Applied for.

Abstract, budget complementation table for R01 CA84950 Molecular Epidemiology of Prostate Cancer InTobagonians.

Abstracts.

1. Patrick AL, Bunker CH, Brufsky AM, Dhir R, Becich MJ. Preliminary screening results suggest high prevalence of prostate cancer in Tobago. Abstract accepted for the Annual Meeting of the Caribbean Health Research Council, April 21-24, 1999, Barbados. (Appendix)
2. Patrick AL, Bunker CH, Konety BR, Brufsky AM, Vivas CA, Dhir R, Becich MJ, Trump DL, Kuller LH. Positive Predictive Value of Prostate Specific Antigen (≥ 4 ng/ml) and Abnormal Digital Rectal Exam for Prostate Cancer on the Caribbean Island of Tobago. Submitted for Annual Meeting of the Caribbean Health Research Council, April 20-22, 2000, Port of Spain, Trinidad & Tobago. (Appendix)
3. Konety BR, Bunker CH, Krill D, Patrick AL, Vivas C, Wagner T, Dhir R, Bastacky S, Brufsky A, Bartoletta R, Trump DL, Kuller L, Becich MJ. Comparison of the features of prostate cancer diagnosed in the United States and in an Afro-Caribbean population. Submitted to the Annual Meeting of the American Urological Association, April 29-May 4, 2000. (Appendix)
4. Bunker CH, Patrick AL, Brufsky AM, Vivas CA, Dhir R, Konety BR, Becich MJ, Trump DL, Kuller LH. High prevalence of psa screening-detected prostate cancer among Afro-Caribbeans: preliminary results from the Tobago prostate cancer survey. Submitted to the Annual Meeting of the American Urological Association, April 29-May 4, 2000. (Appendix)

Presentations.

1. Patrick AL, Bunker CH, Brufsky AM, Dhir R, Becich MJ. Preliminary screening results suggest high prevalence of prostate cancer in Tobago. Abstract accepted for the Annual Meeting of the Caribbean Health Research Council, April 21-24, 1999, Barbados. Presentation made by Dr. Bunker (Appendix)
2. Bunker C. Epidemiology of Prostate Cancer in Populations of African Descent. Presented at A Symposium on Prostate Cancer, University of Pittsburgh Medical Center, June 19, 1999. Target audience: African American clinicians and the general public. (Appendix)

Manuscript.

1. Bunker CH, Patrick AL, Brufsky AM, Vivas CA, Dhir R, Konety BR, Becich MJ, Trump DL, Kuller LH. High Prevalence of PSA Screening-Detected Prostate Cancer Among Afro-Caribbeans: Preliminary Results From the Tobago Prostate Cancer Survey. To be submitted to the Journal of Urology in December, 1999.

Table 1. Tobago Prostate Survey - Annual Summary, Year 1, ending Nov.1, 1999

Age Group	N	PSA			Digital Rectal Exam (DRE)			PSA and/or DRE abnorm	Biopsy			Prost Cancer Among Screened Particip
		to be assayed	< 4 ng/ml	≥ 4 ng/ml (%) ^b	no results ^c	norm	abnorm (%) ^d		to be done	norm	prost canc(%) ^e	
<40	4	2	2	0 (0)	0	4	0(0)	0	0	0	0	0
40-49	230	77	152	1(0.7)	63	156	11(7)	12	7	4	1(20)	0.7
50-59	300	54	212	34(14)	62	205	34(14)	56	21	22	13(37)	5.3
60-69	327	48	184	95(34)	50	210	67(24)	127	39	47	41(47)	14.7
70-79	171	17	74	80(52)	29	82	60(42)	96	32	27	37(58)	24.0
80-89	45	10	14	21(62)	13	9	23(72)	28	13	5	10(67)	28.6
90+	3	0	0	3(100)	0	1	2(67)	3	2	1	0	0
50-79	798	119	470	209(31)	141	497	160(25)	279	92	96	91(49)	13.4
<40-90+	1080 ^a	208	638	234 (27)	217	667	196(23)	322	114	106	102(49)	11.7

^a An additional 8 subjects were recruited for whom age is not yet available(elderly men who could not remember birth date, families being contacted), total recruitment 1088.

^b Percent elevated PSA among all PSA assays.

^c Includes 25 with invalid DRE results, e.g. could not be examined adequately, too obese etc.

^d Percent of valid DRE results which were abnormal.

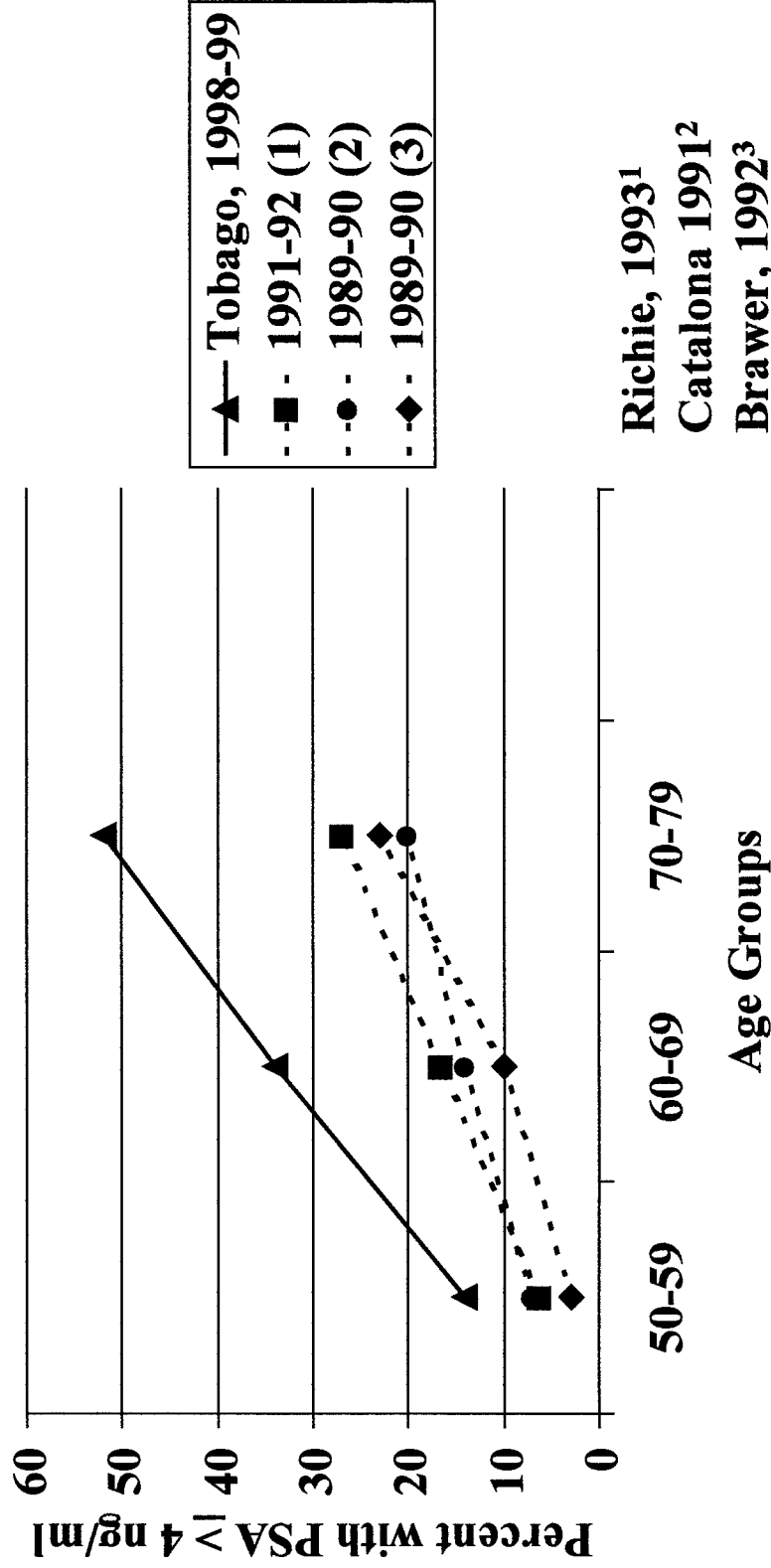
^e Percent positive predictive value for elevated PSA/abnormal DRE.

^f Prostate cancer as a percent of all men with screening results in each age group.

Table 2. Positive Predictive Value of PSA and DRE in Tobago							Page 1
Age Group	Total N	PSA \geq 4		biop		Ca	%ppv
		n	%		%		
40-49	121	1	1%	0	0%	0	
50-59	212	34	16%	20	59%	10	50%
60-69	259	95	37%	69	73%	36	52%
70-79	136	80	59%	55	69%	33	60%
	728	210	29%	144	69%	79	55%
50-59	212	34	16%	20	59%	10	50%
60-69	259	95	37%	69	73%	36	52%
70-79	136	80	59%	55	69%	33	60%
	607	209	34%	144	69%	79	55%
		DRE abn					
		n	%	biop	%	Ca	%ppv
40-49	121	11	9%	5	45%	1	20%
50-59	212	33	16%	22	67%	7	32%
60-69	259	67	26%	48	72%	24	50%
70-79	136	60	44%	48	80%	29	60%
	728	171	23%	123	72%	61	50%
50-59	212	33	16%	22	67%	7	32%
60-69	259	67	26%	48	72%	24	50%
70-79	136	60	44%	48	80%	29	60%
	607	160	26%	118	74%	60	51%
		PSA \geq 4					
		DRE norm					
		n	%	biop	%	Ca	%ppv
40-49	121	1	1%	0	0%	0	
50-59	212	21	10%	12	57%	6	50%
60-69	259	54	21%	38	70%	16	42%
70-79	136	28	21%	13	46%	7	54%
	728	104	14%	63	61%	29	46%
40-49	212	21	10%	12	57%	6	50%
50-59	259	54	21%	38	70%	16	42%
60-69	136	28	21%	13	46%	7	54%
	607	103	17%	63	61%	29	46%

Table 2. Positive Predictive Value of PSA and DRE in Tobago						Page 2	
		DRE abn					
		PSA norm					
		n	%	biop	%	Ca	%ppv
40-49	121	7	6%	5	71%	1	20%
50-59	212	18	8%	11	61%	1	9%
60-69	259	27	10%	19	70%	5	26%
70-79	136	13	10%	8	62%	4	50%
	728	65	9%	43	66%	11	26%
40-49	212	18	8%	11	61%	1	9%
50-59	259	27	10%	19	70%	5	26%
60-69	136	13	10%	8	62%	4	50%
	607	58	10%	38	66%	10	26%
		PSA &/or					
		DRE abn					
		n	%	biop	%	Ca	%ppv
40-49	121	12	10%	5	42%	1	20%
50-59	212	56	26%	34	61%	13	38%
60-69	259	127	49%	88	69%	41	47%
70-79	136	96	71%	64	67%	37	58%
	728	291	40%	191	66%	92	48%
40-49	212	56	26%	34	61%	13	38%
50-59	259	127	49%	88	69%	41	47%
60-69	136	96	71%	64	67%	37	58%
	607	279	46%	186	67%	91	49%
		PSA and					
		DRE abn					
		n	%	biop	%	Ca	%ppv
40-49	121	0	0%	0	#DIV/0!	0	
50-59	212	11	5%	8	73%	4	50%
60-69	259	35	14%	29	83%	19	66%
70-79	136	44	32%	39	89%	25	64%
	728	90	12%	76	84%	48	63%
40-49	212	11	5%	8	73%	4	50%
50-59	259	35	14%	29	83%	19	66%
60-69	136	44	32%	39	89%	25	64%
	607	90	15%	76	84%	48	63%

Figure 1. Percent with Elevated PSA (≥ 4 ng/ml) in Tobago compared with early U.S. screening studies



DESCRIPTION: State the application's broad, long-term objectives and specific aims, making reference to the health relatedness of the project. Describe concisely the research design and methods for achieving these goals. Avoid summaries of past accomplishments and the use of the first person. This description is meant to serve as a succinct and accurate description of the proposed work when separated from the application. If the application is funded, this description, as is, will become public information. Therefore, do not include proprietary/confidential information. **DO NOT EXCEED THE SPACE PROVIDED.**

Preliminary prostate cancer screening data from the Afro-Caribbean population aged 50-79 on the Caribbean island of Tobago revealed a high rate (29%) of elevated PSA (>4ng/ml). Of the 79% undergoing biopsy, 51% were diagnosed with prostate cancer. High incidence of prostate cancer has recently been reported among Afro-Caribbean Jamaicans. These data suggest that the elevated risk for prostate cancer, observed in African Americans, is present in other populations of West African descent. This strongly suggests that prostate cancer risk is influenced by genetic component(s) in combination with lifestyles/metabolic factors common across populations of African descent living in diverse environments. We propose to conduct a molecular epidemiology study of prostate cancer in the Tobago male population, aged 40-79 (n=5121), (92 percent of African descent). We are currently screening the population, aged 50-79 (n=3000) using serum (prostate specific antigen) PSA (>4 ng/ml) and digital rectal exam (DRE). This proposed study will screen men aged 40-49 (n=1800) for elevated PSA (>2ng/ml) or abnormal DRE, in addition to men aged 50-79. We expect to study 300 screening detected cases compared with 300 frequency age matched controls. We will determine whether variants in candidate genes related to sex hormone metabolism, growth factor, vitamin D, PSA transport and toxic substance metabolism, or to loci for familial prostate cancer on chromosomes 1 and X, are associated with prostate cancer, and whether gene frequencies differ from published studies of Caucasian and African American populations. Other molecular markers will include serum arachidonic acid and IGF-1 (for each, hypothesize high levels in cases). Bone mineral density, a surrogate for long term IGF-1 and sex hormone exposure, and central fat distribution will be measured (for each, hypothesize elevated in cases). This large, very cooperative, male population of West African descent, provides a unique opportunity for the study of prostate cancer risk because prostate cancer risk is high, the population is primarily of West African descent, and there is less admixture than among African Americans. Understanding the contribution of environmental, genetic and metabolic factors will lead to measures to reduce the risk for prostate cancer among men of West African descent in the U.S., the Caribbean and other geographic areas.

PERFORMANCE SITE(S) (organization, city, state)

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KEY PERSONNEL

Name	Organization	Role on Project
Clareann H. Bunker	University of Pittsburgh	Principal Investigator
Sheldon I. Bastacky	University of Pittsburgh	Co-Investigator
Michael J. Becich	University of Pittsburgh	Co-Investigator
Adam Brufsky	University of Pittsburgh	Co-Investigator
Rajiv Dhir	University of Pittsburgh	Co-Investigator
Robert E. Ferrell	University of Pittsburgh	Co-Investigator
Badrinath R. Konety	University of Pittsburgh	Co-Investigator
Lewis H. Kuller	University of Pittsburgh	Co-Investigator
Valle Nazar-Stewart	University of Pittsburgh	Co-Investigator
Alan L. Patrick	University of Pittsburgh	Co-Investigator
Clifford J. Rosen	Maine Center for Osteoporosis Research & Education	Co-Investigator
Donald L. Trump	University of Pittsburgh	Co-Investigator

Bunker, Clareann H.

Table 1. Grant Activity Timetable and complementation (no overlap) with Department of Defense Funding (DAMD17-99-1-9015).

Activity	DAMD 11/98- 10/99	DAMD 11/99-9/2000	Grant Y1 10/99-9/2000	DAMD 10/00-4/01	Grant Y2 10/00-9/01	Grant Y3 10/01-9/02	Grant Y4 10/02-9/03	Grant Y5 10/03-9/04	Total for NIH Grant
Initial PSA, DRE									
Age 40-49	--	--	300	--	800	350			1450
Age 50-79	1600	900	--	--	--	--			--
Initial biopsy									
Age 40-49	--	--	30	--	80	35			145
Age 50-79	180	320		150		--			
Hand X-ray, physical activity, food freq									
Initial Recall		200	1000		750	400			2150
Hand X-ray read.	--	200	1000	--	650	800			1450
Rescreening					1400	1200			3600
High risk Controls			650		443	319 500			3250
Total PSA, DRE/yr			950		1242	1169			3361
Rebiopsy/biopsy									
High risk Controls			520		354	255 80			1129 80
Total biopsy/yr			550		434	370			1354
Case control (1050)									
Genetic markers									
5 markers ¹ 12 markers ²		200	200						200
17 markers			75		275	275	225		850
Arachidonic acid ¹	--	200	75		275	275	225		850
Lipids			275		275	275	225		
Serum IGF-1			275		275	275	225		1050

¹ 5 markers and arachidonic acid funded for 200 participants in DAMD pilot study. ² 12 markers funded only in this application. ³ Calculated assuming 80% are biopsied,

Abstract accepted for the Annual Meeting of the Caribbean Health Research Council, April 21-24, 1999, Barbados

Preliminary screening results suggest high prevalence of prostate cancer in Tobago.

Al. Patrick, CH Bunker, AM Brufsky, R Dhir, MJ Becich, Scarborough Regional Hospital, Tobago, Trinidad & Tobago, and University of Pittsburgh, Pittsburgh, PA, USA

Objective: to establish screening parameters for prostate cancer, and to determine whether the prevalence of prostate cancer in the predominantly Afro-Caribbean population on the Island of Tobago is high, compared with Caucasians, as is observed among populations of African descent in Westernized countries.

Design and Methods: All men aged 50-79 (approximately 3000) are invited to participate in a population based screening for prostate cancer, using serum prostate specific antigen (PSA) and digital rectal exam (DRE). Men with elevated PSA (≥ 4 ng/ml) or abnormal DRE are offered an ultrasound guided sextant biopsy of the prostate gland.

Results: To date, PSA levels have been completed in 346 men, mean age 60.4, S.D. 9.3, mean PSA 12.9, S.D. 76.8, median PSA 1.5, range 0.1-1112 ng/ml. The proportion of men with elevated PSA overall was 25.6%, and in age groups 40-49 (0/49, 0%), 50-59 (11/87, 13%), 60-69 (40/115, 35%), and 70-79 (26/51, 51%). Of 25 men with completed biopsy pathology, 15 (60%) were diagnosed with prostate cancer, 10 with Gleason grade 6, grade 7 (3), grade 8 (1), and grade 10 (1). Both the proportion of positive screens, and of positive biopsy are much higher than those observed in Caucasian populations.

Conclusions: We conclude that these preliminary screening results suggest a high risk for prostate cancer in this population of African descent, as is observed among African Americans. Since these two populations presumably experience different environmental exposures, these data support the hypothesis that populations of African descent share genetic and/or lifestyle factors which contribute to their elevated risk for prostate cancer.

Abstract submitted to the Caribbean Health Research Council meeting, April 20-22, 2000, Port of Spain, Trinidad & Tobago

Positive Predictive Value of Prostate Specific Antigen (≥ 4 ng/ml) and Abnormal Digital Rectal Exam for Prostate Cancer on the Caribbean Island of Tobago

AL Patrick, Port of Spain, Trinidad & Tobago, CH Bunker, BR Konety, AM Brufsky, CA Vivas, R Dhir, MJ Becich, DL Trump, LH Kuller, Pittsburgh PA USA

Introduction. Early reports from prostate cancer screening studies in Caucasian men, aged 50-79, observed a positive predictive value (PPV) of approximately 30-40% for elevated (≥ 4 ng/ml) prostate specific antigen (PSA), and approximately 20-30% for abnormal digital rectal exam (DRE).

Methods. We screened 728 men aged 40-79 recruited from the general population on the Caribbean Island of Tobago, Trinidad & Tobago. Ninety-five percent reported African ancestry. This population had not previously undergone screening for prostate cancer. PSA was elevated (≥ 4 ng/ml) and/or DRE was abnormal in 291 (40%) men. Pathological diagnosis of random sextant biopsies has been completed in 191 (66%) men. Ninety-two men were diagnosed with prostate cancer (13% [92/728] of the screened population).

Results. Among men biopsied for abnormal DRE in the presence of normal PSA, PPV for abnormal DRE was 26% (11/43), range 9-50% across age groups. Among men with elevated PSA and normal DRE, the PPV for PSA was 46% (29/63), range 42-54 (no men aged 40-49 (n=105) fell into this category). When all men with elevated PSA were considered, ignoring DRE status, PPV for PSA was 55% (79/144), range 50-60%.

Discussion. The PPV of abnormal DRE was similar to that observed in other populations. In contrast, the PPV of elevated PSA was considerably higher than in other populations undergoing screening for the first time.

Conclusion. The PPV of PSA (≥ 4 ng/ml) was higher than in other populations. We speculate that a lower PSA cutpoint may be appropriate for optimal ascertainment of cases in this high risk population.

Konety, Badrinath

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**The American Urological Association, Inc.® 95th
Annual Meeting**

Presenting Author: Badrinath R Konety

Presentation Type: Paper

Category: 45 Epidemiology and Natural History

Keywords: prostate cancer, African-Americans, epidemiology

**COMPARISON OF THE FEATURES OF PROSTATE CANCER DIAGNOSED IN THE
UNITED STATES AND IN AN AFRO-CARIBBEAN POPULATION..**

Badrinath R Konety; Clareann H Bunker; Diane Krill; Alan L Patrick; Carlos Vivas; Tracie Wagner; Rajiv Dhir; Sheldon Bastacky; Adam Brufsky; Roger Bartoletta; Donald L Trump; Lewis Kuller; and Michael J Becich.

Introduction and Objectives. Prostate cancer incidence is higher in African-Americans (AA) than among Caucasians (C). The features of prostate cancer diagnosed in Afro-Caribbean (T) men who have a similar ethnic origin as AA but different geographic influences are not known. We compared data obtained from an ongoing study of prostate cancer on the island of Tobago to that obtained from the University of Pittsburgh Prostate Cancer Database (UPPCD).

Methods. Age, serum PSA, and biopsy Gleason grade from patients diagnosed with prostate cancer in group T (n=54) were compared to those of a reference population of AA (n=35) and C (n=407), derived from the UPPCD. Patient selection was restricted to the comparable age range of 50-74 yrs in all three groups. PSA and biopsy Gleason grade were not normally distributed (Kolmogorov-Smirnov test) in the three groups. Pair-wise comparisons were performed using the Mann-Whitney U test (non-parametric).

Results. There was no significant difference in age between the three groups (T, AA and C). Median PSA (ng/ml) for the three groups was: 8.0 (T), 9.0 (AA) and 5.9 (C). The mean and median PSA in group AA were significantly higher than that of group C (p<0.001). Median PSA in group T was similar to that of group AA, but the mean and median values were significantly higher than in group C (p<0.0001). Gleason grade distribution in the three groups was: T - 94.4% grade 4-7, 5.6% grade 8-10; AA - 94.3% grade 4-7 and 5.7% grade 8-10; C - 5.7% <4, 85.5% 4-7, 8.8% 8-10.

Conclusions. There are differences in serum PSA at diagnosis and biopsy Gleason grade distribution between African-Americans and Caucasians. However, Afro-Caribbeans and African-Americans appear to have similar Gleason grade distribution and PSA at diagnosis. This may reflect differences in the extent of screening and access to care between Caucasians and the other populations. However, this also demonstrates the similarities in the features of prostate cancer diagnosed in populations of African origin (T and AA) who have similar ethnic backgrounds but different dietary and environmental influences. These data strengthen the possibility of a genetic basis for the increased risk of prostate cancer in populations of African origin.

Source of funding: NIH Grant R01 CA84950-01 and DOD Grant DAMD17-99-1-9015

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The American Urological Association, Inc.® 95th Annual Meeting

Presenting Author: Clareann H Bunker

Presentation Type: Paper

Category: 45 Epidemiology and Natural History

Keywords: prostate cancer, screening, Afro-Caribbean

HIGH PREVALENCE OF PSA SCREENING-DETECTED PROSTATE CANCER AMONG AFRO-CARIBBEANS: PRELIMINARY RESULTS FROM THE TOBAGO PROSTATE CANCER SURVEY.

Clareann H Bunker, Pittsburgh, PA; Alan L Patrick, Port-of-Spain, Trinidad, TTO; Adam M Brufsky, Pittsburgh, PA; Carlos A Vivas, Pittsburgh, PA; Rajiv Dhir, Pittsburgh, PA; Badrinath R Konety, Pittsburgh, PA; Michael J Becich, Pittsburgh, PA; Donald L Trump, Pittsburgh, PA; and Lewis H Kuller, Pittsburgh, PA.

Introduction and Objectives. Risk for prostate cancer is high among African Americans. We hypothesized that risk for prostate cancer is also high in other populations of African descent. Our objective was to determine the screening-detected prevalence of prostate cancer in the predominantly Afro-Caribbean population on the Island of Tobago.


Methods. Male residents aged 50-79 were invited by word of mouth to participate in a population based screening for prostate cancer using serum prostate specific antigen (PSA) and digital rectal exam (DRE). Men with elevated PSA (≥ 4 ng/ml) were offered an ultrasound guided sextant biopsy of the prostate gland.

Results. After excluding two men with previously diagnosed prostate cancer, screening data were analyzed for the first 529 (23%) of 2346 men in the target population. Mean age was 63.1 S.D. 7.7 years, median 63.0 years. Mean PSA 10.2, S.D. 49.5, median PSA 1.8, range 0.1-1112 ng/ml. Elevated PSA was observed in 33% (173/529) overall, and in age groups 50-59 (26/180, 14%), 60-69 (84/230, 37%), and 70-79 (63/119, 53%). Of 117 men biopsied, 63 (54%) (or 12% of the 529 screened) were diagnosed with prostate cancer, 55(87%) with Gleason grade 5-7, 8(13%) with grades 8-10.

Conclusions. These preliminary screening results suggest a high risk for prostate cancer in this population of African descent, as is observed, based on incidence data, among African Americans. Since these populations presumably experience different environmental exposures, these data support the hypothesis that populations of African descent share genetic and/or lifestyle factors which contribute to their elevated risk for prostate cancer.

Source of funding: NIH Grant R01 CA84950-01; DOD Contract DAMD17-99-1-9015

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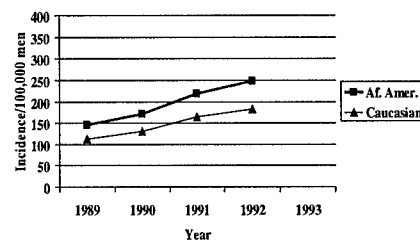
Signature : (Clareann H Bunker)

Preliminary screening results suggest high prevalence of prostate cancer in Tobago.

*AL Patrick, CH Bunker, AM Brufsky,
R Dhir, MJ Becich, Scarborough
Regional Hospital, Tobago, Trinidad
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CHRC April 1999

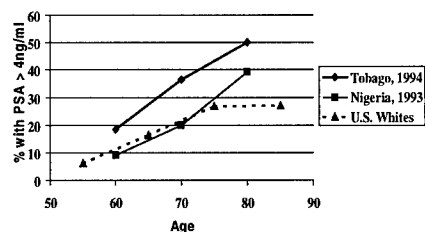
Incidence of Prostate Cancer in the US¹



¹ US data from SEER, 1996

CHRC April 1999

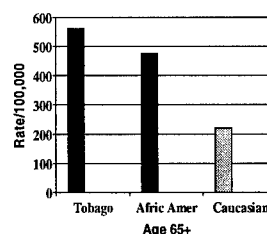
Elevated Serum PSA in Tobago, Nigeria, and U.S. White Populations



U.S.. Whites, Ritchie et al., 1993

CHRC April 1999

Annual Prostate Cancer Mortality/100,000, Tobago, 1990-1994



U S data from SEER, 1988-92, age-adjusted to U S 1970 pop

CHRC April 1999

Tobago Prostate Survey Hypothesis

Prostate cancer risk is elevated in populations of African descent living in diverse environments suggesting an etiological role for genetic factors and/or shared lifestyle factors.

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Tobago Prostate Survey Methods

University of Pittsburgh

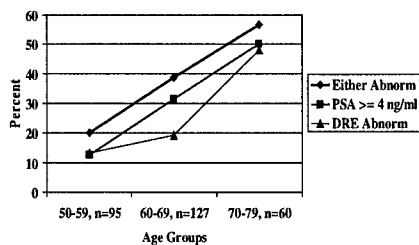
- Recruit male population aged 50-79
- PLCO questionnaire
- PSA assays
- Biopsy support
- Biopsy pathology
- Research followup

Tobago Health Care Syst

- House, sponsor survey
- Laboratory support
- Digital rectal exams
- Perform biopsies
- Provide treatment
- Clinical followup
- Research followup

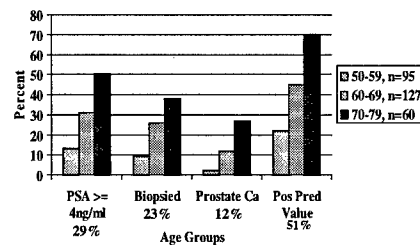
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PSA and DRE Screening, Tobago, January, 1999



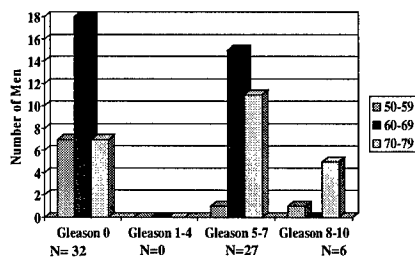
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Prostate Cancer Diagnosis Following PSA Screening, Tobago Jan 1999



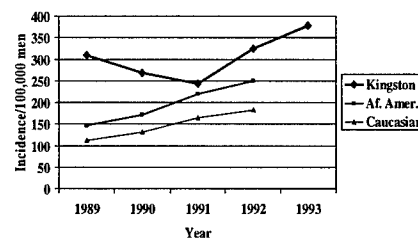
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Distribution of Gleason Scores by Age Group, Tobago, Jan 1999



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Incidence of Prostate Cancer in US and Jamaica¹



¹ Glover et al., 1998; US data from SEER, 1996
CHRC April 1999

Summary, Tobago, Jan 1999

- 282 men aged 50-79 screened, PSA, DRE
- PSA \geq 4 ng/ml, 29% (82 men)
- 80% underwent ultrasound guided random sextant biopsy (65 men) (65/282, 23% of screened)
- 51% of men undergoing biopsy were diagnosed with prostate cancer (33/282, 12% of screened)
- 80% (27/33) of prostate cancers were Gleason 5-7

CHRC April 1999

Limitations

- Study not yet population based
 - bias due to symptomatic volunteers

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Conclusions

- Rates of elevated serum PSA ($\geq 4\text{ng/ml}$), are considerably higher in Tobago than in the U.S.
- The positive predictive value, for prostate cancer, of elevated PSA is high in Tobago
- Prevalence of prostate cancer appears to be considerably higher in Tobago than in the U.S.
- These results suggest serious implications for populations of African descent.

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Tobago Prostate Survey Case-Control Study

- Bone density (hand X-ray)
- serum arachidonic acid
- genetic markers
 - androgen receptor
 - vitamin D receptor
 - 5-alpha-reductase
 - glutathione-s-transferase P1
 - chromosome 1q24-25

CHRC April 1999

Experience with Serum Prostate Specific Antigen (PSA) Screening for Prostate Cancer in men aged 50-79, Tobago, January 1999

Age group	Est well pop	Expected recruitment (80%)		Recruited to date with PSA results		PSA $\geq 4\text{ng/ml}$		biopsied to date age 50-79		prostate Ca diagnosed	
	(a) N	(b) n	b/a	(c) n	c/b	(d) n	d/c	(e) n	e/d	(f) n	f/e
50-59	1332	1066	80%	95	9%	12	13%	10	83%	2	20%
60-69	1007	806	80%	127	16%	40	31%	35	88%	15	43%
70-79	592	474	80%	60	13%	30	50%	23	77%	16	70%
Total	2931	2346	80%	282	12%	82	29%	68	83%	33	49%

CHRC April 1999



University of Pittsburgh
School of Medicine

UPMC HEALTH SYSTEM
Center for Continuing Education
in the Health Sciences

The University of Pittsburgh
Cancer Institute



The National Association for the
Advancement of Colored People,
Pittsburgh Branch

Jointly sponsor

A Symposium on Prostate Cancer

Saturday, June 19, 1999
8:00 AM to 2:45 PM

University of Pittsburgh Medical Center
Conference Center
Scaife Hall Room 1105
200 Lothrop Street
Pittsburgh, PA 15213

Course Director

Adam Brufsky, MD, PhD
Assistant Professor of Medicine
University of Pittsburgh Cancer Institute

Course Description

Prostate cancer is a leading cause of cancer related death and morbidity among all African-American men. This course provides a current update on prostate cancer screening, therapy, and epidemiology in African-American men, with some emphasis on African-Americans.

Objectives:

At the end of the course, the participants should be able to:

- Explain some of the issues and debates concerning screening for prostate cancer in 1999.
- Identify some of the current treatment options available for men with prostate cancer in 1999.
- Report on the epidemiology of prostate cancer in African-Americans and other populations of men of African descent worldwide.
- Discuss some of the issues for further research in prostate cancer screening and therapy in 1999.

Who Should Attend

Physicians, physician assistants, nurses, nurse practitioners, and other health professionals with an interest in prostate cancer.



If you have a disability, advance notification of any special needs will help us serve you better.

Please notify us of your needs at least two weeks in advance of the program.

Parking

Parking available in the University of Pittsburgh Medical Center garage on Terrace Street directly across from Salk Hall.

Faculty

All directors and local faculty are affiliated with the University of Pittsburgh School of Medicine, unless otherwise indicated.

Course Director

Adam Brufsky, MD, PhD
Assistant Professor of Medicine
University of Pittsburgh
University of Pittsburgh Cancer Institute

Guest Faculty

Otis Brawley, MD
Director, Special Populations Research
National Cancer Institutes
Bethesda, Maryland

Ronald A. Morton, Jr., MD
Assistant Professor of Urology
Director of Laboratories, Baylor Prostate Center
Chief of Urology, VA Medical Center, Houston
Baylor College of Medicine
Houston, Texas

Local Faculty

Russell Fuhrer, MD
Medical Director, Mary Hillman Jennings
Radiation Oncology Center
Assistant Professor of Radiation Oncology
UPMC Shadyside

Clareann Bunker, PhD
Assistant Professor
Department of Epidemiology
Graduate School of Public Health

Robert Getzenberg, MD
Assistant Professor
Director of Research
Prostate and Urologic Cancer Center
University of Pittsburgh Cancer Institute

Judith A. Daniels, MMS, PA-C
Physician Assistant, WPIC
Chair, Health Committee
Pittsburgh Branch NAACP

In accordance with Accreditation Council for Continuing Medical Education, requirements on disclosure, information about relationships of presenters with commercial interests (if any) will be included in materials distributed at the time of the conference.

Schedule

8:00 AM	Registration/Continental Breakfast
8:30 AM	Welcome and Introduction <i>Adam Brufsky, MD, PhD</i> <i>Judith A. Daniels, MMS, PA-C</i>
8:45 AM	Prostate Cancer Screening and Chemoprevention <i>Otis Bruley, MD</i>
9:30 AM	Prostate Cancer Diagnosis and Surgical Therapy <i>Ronald A. Morton, Jr., MD</i>
10:15 AM	Break
10:30 AM	The Future of Prostate Cancer: Research Horizons <i>Robert Getzenberg, MD</i>
11:15 AM	Prostate Cancer Radiation Therapy <i>Russell Furber, MD</i>
NOON	Lunch
1:00 PM	Epidemiology of Prostate Cancer in Populations of African Descent <i>Clareann Bunker, PhD</i>
1:45 PM	Medical Therapy of Prostate Cancer-Advanced Disease <i>Adam Brufsky, MD, PhD</i>
2:30 PM	Closing Remarks and Adjournment <i>Adam Brufsky, MD, PhD</i>

Registration Information

You must postmark all registration forms by June 9, 1999 to pre-register for this conference. We cannot guarantee space in the program or any program inclusions for those registrations we receive after this date.

Tuition: \$50.00	Physicians
\$35.00	Residents/Nurses and other health care professionals
\$25.00	Students

Tuition includes:

- Registration and course materials
- Continental breakfast, refreshments and lunch
- Continuing education credit

Payment must accompany registration. You must provide credit card information now. If we do not receive an employer or personal check four weeks after the conference, we will charge the registration fee to the credit card number you provide.

You must put all cancellations in writing. We will completely refund tuition for cancellations we receive two weeks prior to the conference. The UPMC Health System Center for Continuing Education reserves the right to cancel this program if we do not receive a sufficient number of advance registrations. In the case of cancellation, the department will refund registration and/or special event fees only.

Conference Information

For information about this conference please contact:

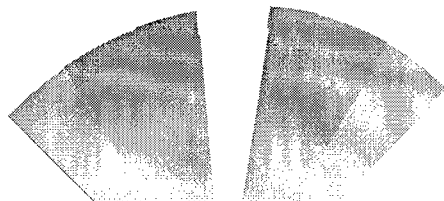
Judith A. Daniels, MMS, PA-C
Conference Planner
Telephone: 412-383-1750
Fax: 412-383-2038
E-mail: danielsja@msx.upmc.edu

Continuing Education Credit

The University of Pittsburgh School of Medicine, as part of the Consortium for Academic Continuing Medical Education, is accredited by the Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians. The Center for Continuing Education in the Health Sciences designates this continuing medical education activity for a maximum of 5.0 hours of Category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the educational activity. Other health care professionals are awarded 0.5 continuing education units (CEUs).

This activity has been planned and implemented in accordance with the Essentials and Standards of the Accreditation Council for Continuing Medical Education through the joint sponsorship of the University of Pittsburgh School of Medicine, Center for Continuing Education in the Health Sciences, the University of Pittsburgh Cancer Institute, and the National Association for the Advancement of Colored People, Pittsburgh Branch.

The University of Pittsburgh, as an educational institution and as an employer, values equality of opportunity, human dignity, and racial/ethnic and cultural diversity. Accordingly, the University prohibits and will not engage in discrimination or harassment on the basis of race, color, religion, national origin, ancestry, sex, age, marital status, familial status, sexual orientation, disability, or status as a disabled veteran or a veteran of the Vietnam era. Further, the University will continue to take affirmative steps to support and advance these values consistent with the University's mission. This policy applies to admissions, employment, access to and treatment in University programs and activities. This is a commitment made by the University and is in accordance with federal, state, and/or local laws and regulations. For information on University equal opportunity and affirmative action programs and complaint/grievance procedures, please contact: William A. Savage, Assistant to the Chancellor and Director of Affirmative Action (and Title IX and 504 Coordinator), Office of Affirmative Action, 901 William Pitt Union, University of Pittsburgh, Pittsburgh, PA 15260, (412) 648-7860.



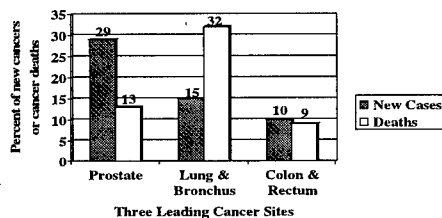
Epidemiology of Prostate Cancer in Populations of African Descent

Clareann H. Bunker, Ph.D.
Department of Epidemiology
University of Pittsburgh

Epidemiology of Prostate Cancer

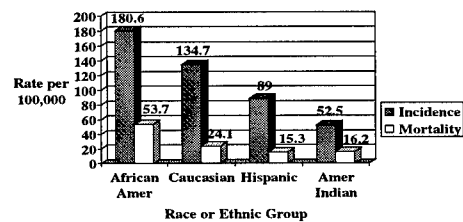
- ▶ African Americans and Whites
 - Incidence
 - Mortality
 - Risk factors
- ▶ Afro-Caribbeans
 - Screening detected prevalence
 - Incidence
- ▶ Other Populations of African descent

Estimated New Cancer Cases and Cancer Deaths, U.S., 1998



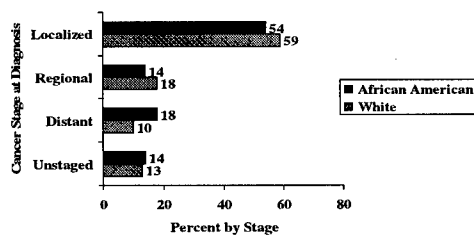
CA 1998;48:14.

Prostate Cancer Incidence and Mortality by Race and Ethnicity, US, 1988-1992



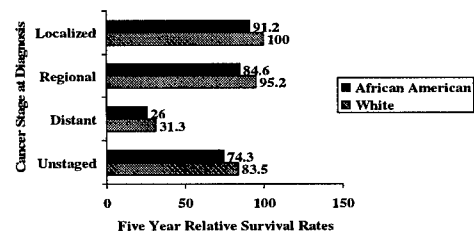
Cancer Facts & Figures -1998, American Cancer Society

Percent Prostate Cancer by Stage at Diagnosis and Race, US, 1986-1993



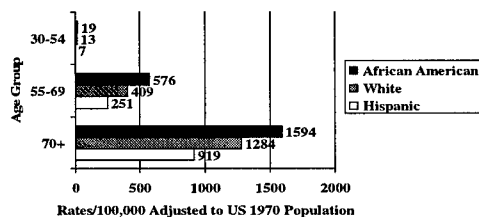
Cancer Facts & Figures -1998, American Cancer Society

Five Year Prostate Cancer Survival by Stage at Diagnosis and Race, US, 1986-1993



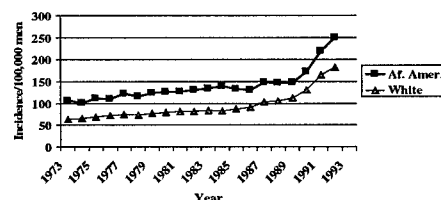
Cancer Facts & Figures -1998, American Cancer Society

Incidence Rates by Age at Diagnosis, 1988-1992



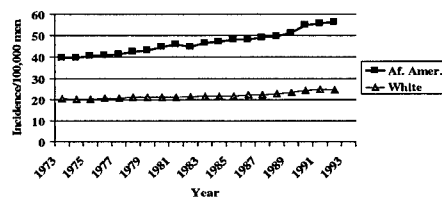
SEER Monograph, NIH Pub 98-4104, 1998

Age-Adjusted Incidence of Prostate Cancer in the US¹



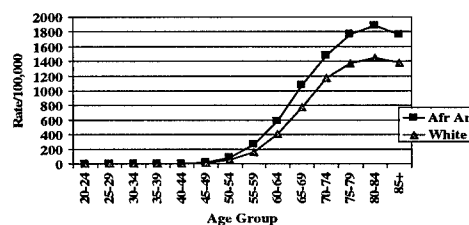
¹ US data from SEER, 1996

Age-Adjusted Mortality Rates for Prostate Cancer in the US¹

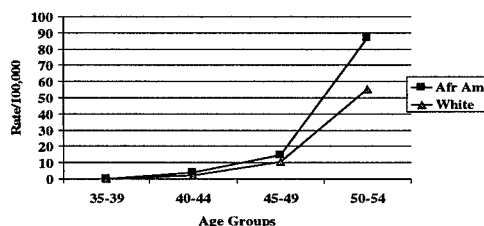


¹ US data from SEER, 1996

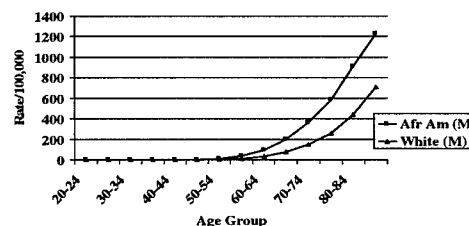
Age Specific Incidence Rates, U.S., 1988-92



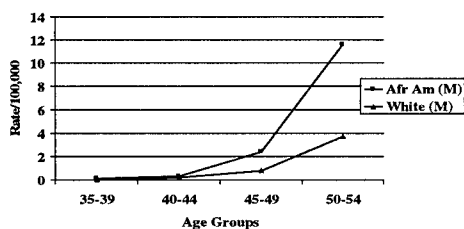
Age Specific Incidence Rates, U.S., 1988-92



Age Specific Mortality Rates, U.S., 1988-92



Age Specific Mortality Rates, U.S., 1988-92



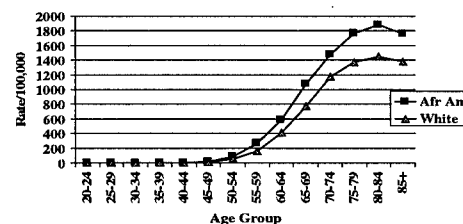
Risk Factors for Prostate Cancer

- ▶ Age
- ▶ Ethnicity
- ▶ Family history of prostate cancer
- ▶ Fat/meat intake
- ▶ Sex hormone metabolism
- ▶ Other - Vitamin D, farming

Risk Factors for Prostate Cancer

- ▶ Age
 - Risk for clinical prostate cancer increases dramatically starting at age 45.
 - At autopsy, much higher rates of preclinical or latent cancer observed - 15-30% of men over the age of 50

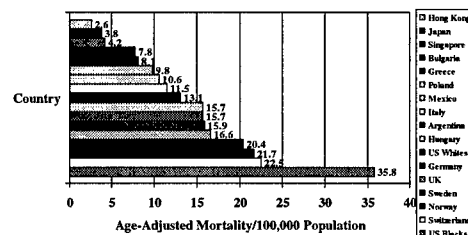
Age Specific Incidence Rates, U.S., 1988-92



Risk Factors for Prostate Cancer

- ▶ Ethnicity
 - At autopsy, rates of preclinical or latent cancer appear to be similar across ethnic groups
 - However, dramatic variation in rates of clinical prostate cancer occurs across ethnic groups/geographic locations
 - Risk increases in populations migrating from low risk areas to high risk areas

Geographic Variation in Age-Adjusted Prostate Cancer Mortality Rates, 1988-91

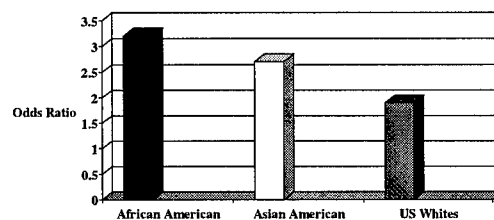


Adapted from Boring et al. Ca Cancer J Clin 1994 and SEER, 1996

Risk Factors for Prostate Cancer

- ▶ Family history of prostate cancer
 - Estimated that about 9% of prostate cancer is of the hereditary form
 - Risk associated with positive family history appears to be similar across ethnic groups

Prostate Cancer Risk with Positive Family History of Prostate Cancer



Whittemore et al. Am J Epidemiol 1995;141:732-40

Risk Factors for Prostate Cancer

- ▶ Fat/meat intake
 - Ecological studies
 - Case-Control studies
 - Longitudinal studies

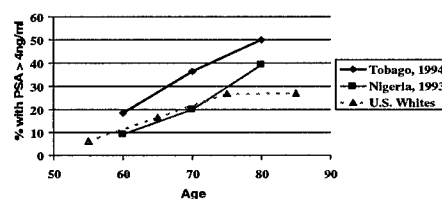
Risk Factors for Prostate Cancer

- ▶ Sex hormone metabolism
 - Sex hormones are not consistently different in prostate cancer cases compared with controls
 - However, prostate cancer is rare in castrated men
 - Testosterone is required for normal prostate development
 - Early prostate cancer is testosterone dependent
 - Some data suggest higher testosterone levels in young black men compared with white men

Risk Factors for Prostate Cancer

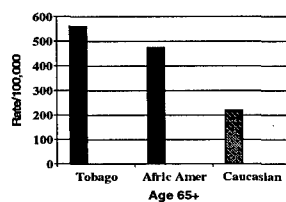
- ▶ Other
 - Vitamin D
 - Farming

Elevated Serum PSA in Tobago, Nigeria, and U.S. White Populations



U.S. Whites, Ritchie et al., 1993

Annual Prostate Cancer Mortality/100,000, Tobago, 1990-1994



U S data from SEER, 1988-92, age-adjusted to U S 1970 pop

Preliminary screening results suggest high prevalence of prostate cancer in Tobago.

AL Patrick, CH Bunker, AM Brufsky, R Dhir, MJ Becich,
Scarborough Regional Hospital, Tobago, Trinidad &
Tobago, and University of Pittsburgh, Pittsburgh, PA,
USA

Tobago Prostate Survey Hypothesis

Prostate cancer risk is elevated in populations of
African descent living in diverse environments
suggesting an etiological role for genetic factors
and/or shared lifestyle factors.

Tobago Prostate Survey Methods

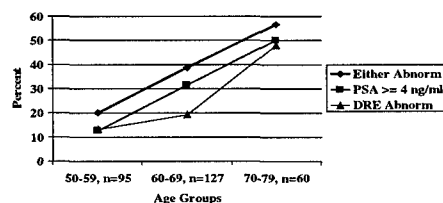
University of Pittsburgh

- Recruit male population aged 50-79
- PLCO questionnaire
- PSA assays
- Biopsy support
- Biopsy pathology
- Research followup

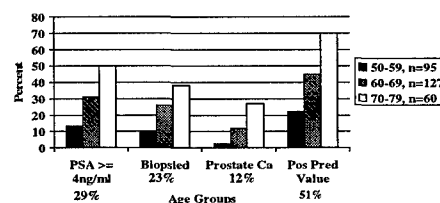
Tobago Health Care Syst

- House, sponsor survey
- Laboratory support
- Digital rectal exams
- Perform biopsies
- Provide treatment
- Clinical followup
- Research followup

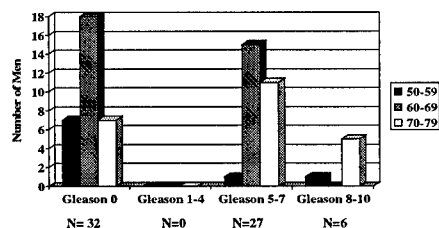
PSA and DRE Screening, Tobago, January, 1999



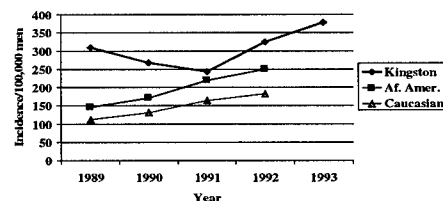
Prostate Cancer Diagnosis Following PSA Screening, Tobago Jan 1999



Distribution of Gleason Scores by Age Group, Tobago, Jan 1999



Incidence of Prostate Cancer in US and Jamaica¹



¹ Glover et al., 1998; US data from SEER, 1996

Summary, Tobago, Jan 1999

- ▶ 282 men aged 50-79 screened, PSA, DRE
- ▶ PSA ≥ 4 ng/ml, 29% (82 men)
- ▶ 80% underwent ultrasound guided random sextant biopsy (65 men) (65/282, 23% of screened)
- ▶ 51% of men undergoing biopsy were diagnosed with prostate cancer (33/282, 12% of screened)
- ▶ 80% (27/33) of prostate cancers were Gleason 5-7

Limitations


- ▶ Study not yet population based
 - bias due to symptomatic volunteers

Conclusions

- ▶ Rates of elevated serum PSA (≥ 4 ng/ml), are considerably higher in Tobago than in the U.S.
- ▶ The positive predictive value, for prostate cancer, of elevated PSA is high in Tobago
- ▶ Prevalence of prostate cancer appears to be considerably higher in Tobago than in the U.S.
- ▶ These results suggest serious implications for populations of African descent.


Prostate Cancer in Nigeria

- ▶ No incidence or mortality data available
- ▶ Hospital data
- ▶ Two year survival about 20%




Summary

- ▶ Prostate cancer occurs more frequently among populations of African descent than among any other populations studied to date
- ▶ Survival after diagnosis of prostate cancer is poorer among African Americans than among white Americans
- ▶ Established risk factors include age, ethnicity, family history, and fat/meat intake.



Conclusions

- ▶ The high rates of prostate cancer observed in populations of African descent living in different environments suggests that shared genes and/or lifestyles are important in the causation of prostate cancer in these populations.



Tobago Prostate Survey Case-Control Study

- ▶ Bone density (hand X-ray)
- ▶ serum arachidonic acid
- ▶ genetic markers
 - androgen receptor
 - vitamin D receptor
 - 5-alpha-reductase
 - glutathione-s-transferase P1
 - chromosome 1q24-25



Clareann H. Bunker

624-3467

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39 slides

Microsoft PowerPoint97 on a Gateway 2000

High Prevalence of PSA Screening-Detected Prostate Cancer Among Afro-Caribbeans:

Preliminary Results From the Tobago Prostate Cancer Survey

Clareann H. Bunker, Ph.D. ¹

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Adam M. Brufsky, M.D., Ph.D. ^{3,6}

Carlos A. Vivas, M.D. ⁴

Rajiv Dhir, M.D. ^{5,6}

Badrinath R. Konety, M.D. ⁴

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⁶ University of Pittsburgh Cancer Institute, Pittsburgh, PA, USA

Running title: Prostate Cancer in Tobago

Abstract.

Objectives: Risk for prostate cancer is high among African Americans. We hypothesized that risk for prostate cancer is also high in other populations of African descent. Our objective was to determine the screening-detected prevalence of prostate cancer in the predominantly Afro-Caribbean population on the Island of Tobago.

Methods: Male residents aged 50-79 were invited by word of mouth to participate in a population based screening for prostate cancer using serum prostate specific antigen (PSA) and digital rectal exam (DRE). Men with elevated PSA (≥ 4 ng/ml) were offered an ultrasound guided sextant biopsy of the prostate gland.

Results: After excluding two men with previously diagnosed prostate cancer, screening data were analyzed for the first 529 (23%) of 2346 men in the target population. Mean age was 63.1 S.D. 7.7 years, median 63.0 years. Mean PSA 10.2, S.D. 49.5, median PSA 1.8, range 0.1-1112 ng/ml. Elevated PSA was observed in 33% (173/529) overall, and in age groups 50-59 (26/180, 14%), 60-69 (78/230, 34%), and 70-79 (63/119, 53%). Of 117 men biopsied, 63 (54%) (or 12% of the 529 screened) were diagnosed with prostate cancer, 55(87%) with Gleason grade 5-7, 8(13%) with grades 8-10.

Conclusions: These preliminary screening results suggest a high risk for prostate cancer in this population of African descent, as is observed, based on incidence data, among African Americans. Since these populations presumably experience different environmental exposures, these data support the hypothesis that populations of African descent share genetic and/or lifestyle factors which contribute to their elevated risk for prostate cancer.

Bunker CH et al., Prostate Cancer in Tobago, draft manuscript, D:\DATA\WORD
DOCS\MANUSCRIPTS\TOBPREVMAN1099BADRIUNLINED.DOC November 24, 1999 (09:49PM)

Key Words: prostate cancer, screening, Afro-Caribbean, prostate specific antigen.

Introduction.

Prostate cancer is a very serious personal and public health problem. Based on 1990-92 data from the U.S. Cancer Surveillance Program (SEER) of the National Cancer Institute, about 1 in 6 men (18.6% of whites, 16.3% of blacks) have a lifetime risk of being diagnosed with prostate cancer, and 3.5% of whites and 4.5% of blacks have a lifetime risk of dying from prostate cancer.¹ Age-adjusted data establish that incidence of prostate cancer is 36% higher, and the mortality rate from prostate cancer is two-fold higher, among persons of African descent compared with Caucasians. Incidence of prostate cancer has risen dramatically in both groups since the late 1980's reflecting the earlier diagnosis which has occurred with the increasing use of serum prostate specific antigen (PSA) testing in the U.S.¹

Established risk factors for prostate cancer include age, ethnicity, family history of prostate cancer, and high fat or meat diet (reviewed by Ross and Schottenfeld).² Other factors suspected include hormone metabolism,^{3 4} Vitamin D metabolism,⁵ and a few occupational exposures⁶. The relationships of a number of candidate genes to prostate cancer are under investigation with most published results limited to Caucasian populations⁷. The reasons for the higher risk for prostate cancer among African Americans are unknown.

Until recently, there has been little solid prevalence, incidence or mortality data for populations of African descent outside the U.S., though data published a few years ago in an annual summary of worldwide data suggested high rates of prostate cancer mortality in Martinique and Trinidad & Tobago.⁸ In 1998, Glover et al. reported high rates of prostate cancer incidence in the predominantly Afro-Caribbean population of Jamaica.⁹ Data regarding

screening parameters and prevalence of prostate cancer in populations of African descent in the U.S are sparse,^{10 11} and virtually absent in other populations of African descent.

We hypothesize that risk for prostate cancer is high among populations of African descent living in diverse environments. If so, this would suggest that populations of African descent share genetic and/or lifestyle factors which increase risk for prostate cancer.

On the Island of Tobago, Trinidad & Tobago, we are embarking on a population-based, longitudinal study of prostate cancer in the male population aged 50-79. Here we are reporting preliminary data from the initial cross-sectional screening using serum prostate specific antigen (PSA) and digital rectal exam (DRE). This study will allow estimation of screening parameters, and prevalence. Longitudinal followup screening is planned to estimate incidence. A nested study of cases and controls will be conducted to investigate the influence of family history, body weight and body weight distribution, meat intake markers, sex hormone markers, occupational exposures, and a number of candidate genetic markers for prostate cancer risk.

Materials and Methods.

Population. The island of Tobago is about 7 by 29 miles in size. According to the 1990 census¹² of Trinidad & Tobago, the male population of Tobago, aged 50-79, numbered 3217. Ninety-two percent of Tobago residents reported that they were of African descent. Most health care is provided by a government supported system through the Tobago Regional Health Authority which manages the 19 neighborhood health centers and one hospital. Some residents travel to Trinidad for specialized care under the government system. Some care is provided by

private care givers. PSA testing has been available but generally limited to symptomatic men seeking care in the private sector.

Recruitment. In the population-based study, each of the seven counties on the island will be the focus of a concentrated sequential recruitment effort for 2-3 months beginning in St. David County, where previous population-based studies have been conducted. Informing by health care workers at the hospital and health centers, posters, flyers, public service announcements, and word of mouth will be the primary methods. House-to-house visits will be used if necessary. The 1990 Census provided the denominator for evaluation of recruitment. It is estimated that approximately 2931 of 3217 male residents aged 50-79 are ambulatory, free-living, non-terminally ill men not previously diagnosed with prostate cancer, and of these, at least 80 percent or 2346 are potential participants in the baseline PSA and DRE screening.

For the preliminary studies reported here, participants entered into the study without any active recruitment efforts, and very little publicity other than word of mouth. Most of the men resided in or near the town of Scarborough where the study is based.

Informed consent. Consent was obtained using forms and procedures approved by the University of Pittsburgh Institutional Review Board and the Tobago Ministry of Health.

Data collection. Data were collected by the locally resident study staff at the study office located at the Tobago Regional Hospital. Data collected include ethnicity, education, occupation, smoking, medical history, personal and family cancer history, vasectomy, prostate symptoms, health screening history, alcohol intake, detailed occupational history, and height, weight, waist and hip measurements.

Biological sample collection. A 15 ml plain vacutainer of peripheral blood was drawn from fasting subjects. Aliquots of serum were frozen at -20°C for later measurement of PSA.

Digital rectal examination (DRE). A systematic DRE was performed by a physician trained according to the study protocol. This exam was scheduled after the blood draw in order to avoid an artifactual increase in serum PSA which may follow digital manipulation of the gland.

PSA measurement. Serum PSA levels were measured at the University of Pittsburgh Central Pathology Laboratory using the automated Microparticle Enzyme Immunoassay, Abbot AxSYM PSA assay (Abbott Laboratories, Abbott Park, IL, USA).

Criteria for referral for prostate biopsy. In the population-based study, subjects will be referred to the Tobago Regional Hospital for biopsy if the DRE is abnormal (except for simple enlargement without palpably abnormal areas) or if serum PSA is elevated (>4.0 ng/ml).

However, in the preliminary study reported here, resources were limited. Thus, only those with elevated PSA levels were referred for biopsy since the predictive value for elevated PSA is reported to be higher than the predictive value for abnormal DRE.¹³ Biopsy was deferred for twenty men with $\text{PSA} < 4$ ng/ml and abnormal DRE.

Prostate biopsy. Prostate biopsies were performed by urologists, or by surgeons trained by urologists from the University of Pittsburgh Medical Center. Trans-rectal ultrasound guided biopsy was performed using an 18 gauge, 21 cm spring-loaded biopsy needle (Boston Scientific, Natick MA). Random sextant biopsies, plus biopsy of suspicious nodules, were obtained according to a standard protocol.

Prostate pathology. The formalin preserved specimens were stored at room temperature and shipped to the University of Pittsburgh for histopathologic examination. The specimens were examined for presence or absence of high grade prostatic intra-epithelial neoplasia (PIN), presence or absence of cancer, Gleason score of cancer, location of cancer, and peri-neural invasion.

Data analysis. Age-specific rates/100 were calculated. Age-standardized rates/100, standard error/100, and 95% confidence intervals were calculated¹⁴ based on the age distribution of a large screened U.S. population.¹⁵

Results.

Of the first 531 men, aged 50-79 who have undergone PSA screening, two (PSA, 88 and 386 ng/ml) reported a previous diagnosis of prostate cancer and were eliminated from analysis. Here, we are reporting on the remaining 529 men. Mean age was 63.1 years, S.D. 7.7, median 63.0, range 50-79. African descent was reported by 94% of the men, and mixed African descent by 3%. Eighteen percent had completed secondary school or higher education. Thirty-eight percent reported ever smoking, while 8% were current smokers.

Fifty-one (10% of 51/529) of the men reported that a physician had told them they had benign prostatic hypertrophy. Seventy percent reported symptoms of benign prostatic hypertrophy. In response to the question, during the past three years, have you had a blood test for prostate cancer, for example PSA, 49 responded yes, once and 10 responded yes, more than once.

Mean PSA was 10.2 ng/ml, S.D. 49.5.2, median PSA 1.8 (numbers changed in accordance with those in abstract. Which ones are correct?), range 0.1-1112 ng/ml. Elevated serum PSA levels (≥ 4 ng/ml) were observed in 173/529 men (33%) (Tables 1). Of 117 men with elevated PSA who underwent biopsies, 63 (54%) were diagnosed with prostate cancer. Those diagnosed with prostate cancer were 12% (63/529) of the population screened. All Gleason scores were 5 or greater, including 55 with Gleason score 5-7, and 8 with Gleason score 8-10 (Table 2). [If one were to consider that men with Gleason score of 5-7, PSA < 20 ng/ml, and age < 70 years, would be candidates for curative therapy such as radical prostatectomy, 15 of 34 men (44%) would fall into this category](Table 2). This statement is not true in the US since all men who were thought to have organ confined disease irrespective of PSA or Gleason grade would be candidates for radical prostatectomy and those thought to have only regional disease would be candidates for radiotherapy, both of which are curative therapies. We segmented patients with Gleason <7 and PSA <20 only because it would not be practical to do surgery or radiotherapy on all in T&T. I am sure the reviewers will criticize this

To examine the influence of possible prior PSA screening, the data were reanalyzed excluding the (? still true or are there more now with the additional data?)59 men reporting a previous blood test for prostate cancer, and 10 who did not know or for whom the data were missing. Among the remaining 460 men, the results were very similar to the total population. PSA was elevated in 173, and prostate cancer was diagnosed in 63 of 117 men biopsied, yielding 13.6 percent (63/460) of those screened diagnosed with prostate cancer.

[Further, when we excluded men who reported symptoms of benign prostatic hypertrophy, the resulting number remaining was small (n=64), and younger than the full cohort, but the outcome was still the same, with 11% (5/64) diagnosed with prostate cancer] – why were men symptomatic for BPH excluded?.

Comment.

This study, which we believe is the first involving screening a large Afro-Caribbean population, found high rates of elevated PSA (≥ 4 ng/ml), ranging from 14%, age 50-59, to 53%, age 70-79. Similar data from screening of other populations of African descent have not been published. In Figure 1, the Tobago data are compared with data from screening studies of predominantly Caucasian populations^{15 16 17} which were conducted between 1989-1992, when PSA screening was just beginning to be widely used in the United States. Age-specific rates of elevated PSA levels in Tobago were approximately double those observed in a large, predominantly Caucasian study in the United States by Ritchie et al.¹⁵ In that volunteer population of 6,630 (92% Caucasian, 3% African American, 5% other), recruited by advertisement, mean age was 62.8 years, and 53% reported symptoms of prostatism. The proportion with elevated PSA (>4 ng/ml) ranged from 6.3% (150/2381) age 50-59, 16.5% (487/2959) age 60-69, to 26.8% (311/1611) in age 70-79 (See figure 1). The standardized rates of elevated PSA, based on the age distribution of the population reported by Ritchie et al., were 27.5/100, standard error 2.53/100 (95% confidence interval, 22.5-32.5/100) in the Tobago population, and 14.8%, standard error, 0.43/100 (95% confidence interval, 15.4-17.85/100) ?? need to recalculate the CI and rates with new data in the population reported by Ritchie et al.¹⁵

As has been observed in African American populations, the positive predictive value of elevated PSA was high in the Tobago population among whom prostate cancer diagnosed in 54% of men undergoing biopsy. In a community based study of relatively young African Americans, aged 40+, mean age 54.9, PSA was over 4 ng/ml in 8% (85/1105)¹⁸. Prostate cancer was diagnosed in 36 of 81 (44%) undergoing biopsy. In a study of 752 men (age not specified) who had undergone biopsy for a history of elevated PSA (≥ 4 ng/ml), cancer rates were 54% (94/175) among blacks and 41% (122/197) among whites¹⁹. In the population of 6630 (92% Caucasian) population reported by Richie et al¹⁵ described above, among the participants with elevated PSA who underwent biopsy, 31% (216/686) over all ages were positive for cancer. The proportion with positive biopsy in that study varied little across age groups (range 29.5-33.8%).

Limitations. A high prevalence of prostatitis could inflate the proportion of men with elevated PSA levels. We did not have the resources to offer repeat PSA testing, either with or without a course of antibiotic treatment to men with elevated PSA. However, the high positive predictive value of elevated PSA level for prostate cancer suggests there were not an undue number of false positives.

Because the participants in this preliminary study were self-referred, and not population based, rates of elevated PSA, and rates of positive biopsy, could be biased toward higher than true rates due to possibly higher self referral rates among men already symptomatic with prostate cancer. However, even the studies reported above, which appear to be the best studies available for estimating these rates, were also strongly influenced by self-referral. Symptoms were

common in the population reported by Richie et al.¹⁵ Furthermore, most of the Tobago cases diagnosed were of moderate grade (87% (55/63) were Gleason grade 7 or lower) [so that it was more likely that symptoms, if present, were due to other causes, e.g. prostatic hypertrophy, than to prostate cancer are symptoms related to Gleason grade of tumor. They may be related to stage of tumor. I am not sure we can make this statement]. Thus it seems likely that prevalence of prostate cancer is truly high in Tobago though this remains to be confirmed by the full population based study.

It should be noted that one concern regarding screening for prostate cancer centers on diagnosing an excess number of cases in the very early stages. This can arouse anxiety before curative treatment would be recommended or is proven to be beneficial. However, among the biopsies completed to date, none of the cases have been in this "too early" stage. this would depend on clinical stage and since we don't have that info it would be hard to make this determination..

Conclusions.

The higher risk for prostate cancer among African Americans compared with Caucasians is well established based on incidence and mortality data¹. Incidence data for prostate cancer in Tobago are not available, and mortality data would be based on small numbers. However, we are able to conclude that the risk for prostate cancer is also high in the Tobago population based on the screening-ascertained prevalence of prostate cancer which is approximately two-fold higher than observed among Caucasian participants in screening studies conducted in a generally similar manner. High risk for prostate cancer was also recently reported in Jamaica based on

high incidence rates⁹. Since these U.S. and Caribbean populations presumably experience different environmental exposures, these data support the hypothesis that populations of African descent share genetic and/or lifestyle factors which contribute to their elevated risk for prostate cancer. Understanding the contribution and interaction of environmental, genetic and metabolic factors may lead to measures to reduce the risk for prostate cancer among men of West African descent in the Caribbean, the U.S., and other geographic areas.

Table 1. PSA Screening Results by Age Group on the Island of Tobago, Trinidad & Tobago, 1997-1998

Age	N(% of	Mean	Std.Dev.	Median	PSA	PSA 4.0-9.9 ng/ml		PSA 10+ ng/ml		Total No. Ca/	Ppn (%) of
Group	total)	PSA	PSA	PSA	0.1-3.9	Prostate		No.(%)	No.(%)	Total No.	screened
		ng/ml	ng/ml	ng/ml	ng/ml	No.(%)	Ca/ Biopsy	No.(%)	prostate Ca/	Biopsy (%)	dx'd
					No.(%)	No.(%)		Biopsy			prostate Ca
50-59	95(34)	2.3	4.9	1.3	83(87)	10(11)	3/9(33)	2(2)	0/1(0)	3/10(30)	3/95(3)
60-69	126(45)	5.7	23.1	1.9	87(68)	29(23)	10/26(38)	10(8)	6/8(75)	16/34(47)	16/126(13)
70-79	59(21)	47.2	172.7	3.8	30(50)	10(17)	2/7(29)	19(33)	13/16(87)	15/22(68)	15/59(25)
Total	280(100)	13.3	82.2	1.7	200(71)	49(18)	15/42(36)	31(11)	19/24(79)	34/66(52)	34/280(12)

Table 2. PSA Levels and Gleason Scores Among Biopsied Men With PSA \geq 4 ng/ml

Age Group	Benign Biopsy		Gleason Score 5-7		Gleason Score 8-10		Total
	PSA < 20	PSA \geq 20	PSA < 20	PSA \geq 20	PSA < 20	PSA \geq 20	
	ng/ml	ng/ml	ng/ml	ng/ml	ng/ml	ng/ml	
50-59	7	0	2	0	1	0	10
60-69	18	0	13	3	0	0	34
70-79	6	1	5	5	1	4	22
Total	31	1	20	8	2	4	66

Revised Table 1. PSA Screening Results by Age Group on the Island of Tobago, Trinidad & Tobago, 1997-1999

Age Group	N(% of total)	Mean PSA ng/ml	Std.Dev. PSA ng/ml	Median PSA ng/ml	PSA 0.1-3.9 ng/ml	PSA 4.0-9.9 ng/ml Prostate No.(%) Ca/ Biopsy No.(%)	PSA 10+ ng/ml No.(%) prostate Ca/ Biopsy No.(%)	Total No. Ca/ Biopsy (%)	Ppn (%) of screened dx'd prostate Ca
50-59	180(34)	2.3	4.0	1.3	154(86)	22(12) 7/15(47)	4(2) 1/1(100)	8/16(50)	8/180(4)
60-69	230(44)	9.5	36.9	2.1	146(64)	58(25) 16/42(38)	26(11) 13/17(76)	29/59(49)	29/230(13)
70-79	119(22)	23.9*	90.3*	4.0	56(47)	31(26) 8/18(44)	32(27) 18/24(75)	26/42(62)	26/119(22)
Total	529(100)	10.2*	49.5*	1.8	356(67)	111(21) 31/75(41)	62(12) 32/42(76)	63/117(54)	63/529(12)

*excluding three men with PSA > 1000 ng/ml

Revised Table 2. PSA Levels and Gleason Scores Among Biopsied Men With PSA \geq 4 ng/ml

Age Group	Benign Biopsy		Gleason Score 5-7		Gleason Score 8-10		Total
	PSA	PSA	PSA	PSA	PSA	PSA	
	< 20 ng/ml	\geq 20 ng/ml	< 20 ng/ml	\geq 20 ng/ml	< 20 ng/ml	\geq 20 ng/ml	
50-59	8	0	7	0	1	0	16
60-69	30	0	21	7	1	0	59
70-79	14	2	13	7	1	5	42
Total	52	2	41	14	3	5	117

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26 Aug 02

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